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## From the trenches: inpatient management of coronavirus disease 2019 in pregnancy



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The novel coronavirus disease 2019 caused by the severe acute respiratory syndrome coronavirus 2 has become a pandemic. It has quickly swept across the globe, leaving many clinicians to care for infected patients with limited information about the disease and best practices for care. Our goal is to share our experiences of caring for pregnant and postpartum women with novel coronavirus disease 2019 in New York, which is the coronavirus disease 2019 epicenter in the United States, and review current guidelines. We offer a guide, focusing on inpatient management, including testing policies, admission criteria, medical management, care for the decompensating patient, and practical tips for inpatient antepartum service management.

**Key words:** coronavirus disease in pregnancy, COVID-19 in pregnancy, critical care in pregnancy, critical care obstetrics, infectious disease in pregnancy, management of COVID-19

### Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread dramatically around the world, but there have been little evidence-based data to guide clinical management of patients with coronavirus disease 2019 (COVID-19) and even less on the management of obstetrical patients. It is known that the spectrum of diseases attributed to COVID-19 is wide, including asymptomatic infection, mild upper respiratory disease, pneumonia, severe respiratory distress, and death.<sup>1</sup> Common presenting symptoms include fever, dry cough, dyspnea, chest pain or tightness, fatigue, and myalgias. Less commonly, pregnant women may report headache, confusion, rhinorrhea, sore throat, hemoptysis, vomiting, and diarrhea.<sup>1</sup> Anosmia or ageusia with COVID-19 has also been reported. The incubation period from exposure to symptom onset is 4 to 5 days, with a range of 2 to 14 days.<sup>1,2</sup>

Initial data suggest that pregnant women are not more susceptible to SARS-CoV-2 infection than nonpregnant patients. However, physiological and anatomic changes associated with

pregnancy may predispose patients to an increased risk for respiratory failure.<sup>3</sup> Patients with comorbidities, such as asthma or other chronic lung disease, cardiovascular disease, hypertension, HIV or other immunocompromised patients, body mass index of  $>40 \text{ kg/m}^2$ , pregestational diabetes, chronic kidney disease, and liver disease may have more significant adverse outcomes compared with healthy pregnant women.<sup>1</sup> Similar to maternal outcomes, there is limited information on fetal and pregnancy outcomes in women with COVID-19. Previous data from severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) pandemics illustrated an increase in miscarriage, stillbirth, and preterm or small-for-gestational-age infants.<sup>1</sup> Data are currently being collected to determine whether COVID-19 infection indicates similar trends. It should also be noted that high fever, which is a common symptom of COVID-19, during the first trimester of pregnancy can increase the risk for certain birth defects.<sup>1</sup>

This article is intended to bring together guidelines from governmental and professional organizations and from the authors' clinical experiences. The recommendations provided below are evidence based where possible; however, most recommendations have been derived from the authors' clinical experience and recommendations from infection control experts. It is also important to note that guidelines are in constant flux as we learn more about SARS-CoV-2 and its clinical manifestations. It is recommended that those taking care of patients with COVID-19 frequently refer to the updates provided on the websites of the Centers for Disease Control and Prevention (CDC), the World Health Organization, the Society for Maternal-Fetal Medicine (SMFM), and the American College of Obstetricians and Gynecologists (ACOG) for the most current recommendations.

### Testing

First-line testing is performed using reverse transcription polymerase chain reaction for SARS-CoV-2 with a nasopharyngeal swab. The test has a high specificity and moderate

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**TABLE 1**  
**Checklist for COVID-19 screening<sup>a</sup>**

Step 1: Ask each patient and visitor the following questions ("Yes" to any question indicates positive screen).

- ☐ Have you been diagnosed as having COVID-19?
- ☐ Have you been exposed to someone with known or suspected COVID-19 in the last 14 days?
- ☐ Have you recently had or do you currently have any 1 of the following?
  - ☐ Subjective or measured fever ( $>100.0^{\circ}\text{F}$ )
  - ☐ Chills
  - ☐ Cough
  - ☐ Shortness of breath
  - ☐ Sore throat
  - ☐ Diarrhea
  - ☐ Malaise or myalgia
  - ☐ Headache
  - ☐ Congestion or runny nose
  - ☐ Loss of taste
  - ☐ Loss of smell

Step 2: Measure the temperature (temperature of  $\geq 100.0^{\circ}\text{F}$  indicates positive screen).

- ☐ Take the temperature of all patients who present to the hospital at entry if possible or at presentation to triage or labor and delivery units and their support person.

This is an alternative screening checklist when resources are not available for universal screening.

COVID-19, coronavirus disease 2019.

<sup>a</sup> If your institution has the resources, consider sending a test for severe acute respiratory syndrome coronavirus 2 infection for all patients who present to the triage or labor and delivery units.

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sensitivity (60%–80%).<sup>4</sup> Swabbing of the nasopharynx is the preferred choice for swab-based testing owing to increased detection rates.<sup>1</sup>

The CDC currently recommends that clinicians use their judgment to determine whether a patient should be tested.<sup>1</sup> In our experience, universal testing of patients and partners has helped identify asymptomatic carriers, likely limiting the spread of the virus and minimizing exposure to staff and other patients. Women may present for admission with routine obstetrical complaints and subsequently develop symptoms of COVID-19 during their hospitalization. Thus, consideration should be given for universal testing of patients admitted to labor and delivery units<sup>5,6</sup> based on the prevalence of the disease in the local community<sup>7</sup> and institutional resource availability.

Resource limitations including test availability and result time may be prohibitive, in which case clinical judgment should be used. An alternative to universal testing includes using intentionally broad screening criteria and testing all patients who have COVID-19–related symptoms, are febrile (temperature of  $>100.0^{\circ}\text{F}$ – $100.4^{\circ}\text{F}$ ), or have epidemiologic risk factors (Table 1). Symptoms of COVID-19 overlap with those of influenza and other viral respiratory diseases; thus, concomitant testing for these infections may be considered under certain circumstances. Anecdotal experience has also

indicated that consideration could be given to test patients on a case-by-case basis who have an intrapartum or postpartum fever, suspected preeclampsia with severe features, and hemolysis, elevated liver enzyme levels, and low platelet levels (HELLP) syndrome owing to the overlap with COVID-19 features.

The variable laboratory turnaround time for SARS-CoV-2 test results needs to be taken into consideration when constructing testing protocols. With rapid testing becoming increasingly available, one should consider using this test for mildly ill or asymptomatic patients. However, some laboratories have longer turnaround times. For those patients with a high clinical suspicion for COVID-19, it may be prudent to treat them as such while awaiting test results. For patients with a high clinical suspicion for COVID-19 and no obvious alternative diagnosis, but a negative result for SARS-CoV-2, continuation of isolation precautions is prudent and repeat testing may be considered. This is because of the relatively high false-negative rate of approximately 30%.<sup>4</sup>

## Inpatient management

### Admission

All patients who present to the hospital should be screened for SARS-CoV-2 infection (Table 1). As per recently published SMFM guidelines, admission to the hospital may be prudent for pregnant women who have a positive result for COVID-19 and have moderate to severe symptoms (tachypnea, dyspnea, refractory fever, oxygen saturation of  $<95\%$ ), clinical findings suggestive of more significant disease (pneumonia, abnormal blood gas tests), findings warranting pharmacologic treatment, or have comorbid conditions that increase risk for a more severe clinical course (Table 2).<sup>8</sup> In addition, patients who do not have the ability to self-isolate at home, for example, undomiciled patients, may also be considered for admission.<sup>1</sup> Patients meeting any admission criteria may need intensive monitoring and should be considered for admission for a minimum of 24 to 48 hours to determine the severity of their current status and potential for disease progression. The degree of hypoxemia based on oxygen saturation levels has been used in many algorithms to determine whether a nonpregnant patient should be admitted for supportive care and observation or discharged home. However, the thresholds used for nonpregnant adults are not appropriate during pregnancy given the oxygen requirement of the fetus necessitates a maternal oxygen saturation of  $\geq 95\%$ .<sup>3</sup>

All patients admitted to the hospital should have basic laboratory and imaging tests performed during their initial evaluation (Table 3). On admission, contact and droplet isolation precautions should be implemented in the patient's inpatient room (Table 4). For patients with hypoxia ( $\text{SpO}_2 < 95\%$ ), D-dimer, procalcitonin, ferritin, lactate dehydrogenase (LDH), and troponin levels should be checked (Table 5). If the clinical presentation is concerning for bacterial superinfection, obtaining a sputum culture and blood culture should be considered. Fluid status, with hourly evaluation of intake and output, should be monitored and volume overload avoided.

Multidisciplinary discussions should be conducted with representation from obstetrics, anesthesiology, pediatrics, and nursing to plan for the next steps in patient management. Practical tips for antepartum service management are presented in Table 6.

### Laboratory and imaging findings

The vast majority of what is known about SARS-CoV-2 infection is derived from data collected from the general population. Specific information relating to pregnant women is limited and the following must be considered with caution.

Lymphopenia is common in patients infected with SARS-CoV-2 and has been reported in up to 83% of cases in nonpregnant individuals.<sup>1</sup> In nonpregnant patients, greater illness severity has been associated with severe lymphopenia and neutrophilia. Illness severity is also associated with increased liver enzymes, LDH, C-reactive protein (CRP), and ferritin.<sup>1</sup> In general, critically ill patients have high plasma levels of inflammatory markers, suggesting that immune dysregulation may play an important role in disease severity and progression. Procalcitonin level may be normal on admission but has been noted to be increased in patients with COVID-19, particularly among those requiring admission to the intensive care unit.<sup>1</sup> It is important to note that markers of inflammation such as CRP can be mildly elevated during normal pregnancy (Table 7).<sup>5</sup> Anecdotally, we have noted that CRP levels of >10 mg/L have correlated with more significant disease and tends to increase or decrease with worsening or improvement of the disease course. However, there are currently no reference levels related to CRP and COVID-19 infection in pregnancy in the literature.

The laboratory findings that have been indicated to be poor prognostic factors in the general population include elevated CRP level, elevated procalcitonin level, thrombocytopenia (platelet count of <100,000/ $\mu$ L), and laboratory evidence of disseminated intravascular coagulation (DIC).<sup>9–11</sup>

Findings on chest x-ray suggestive of COVID-19 include bilateral air space consolidation and bilateral or multilobar infiltrates.<sup>1</sup> The appearance is often noted to have patchy reticular or reticulonodular opacities. However, x-ray findings may be minimal in early disease and often lag behind the clinical findings.<sup>1</sup>

Computed tomography (CT) scan findings typically include bilateral, peripheral ground-glass opacities.<sup>1</sup> Currently, the American College of Radiology does not recommend CT scan for screening or first-line testing in the diagnosis of COVID-19.<sup>12</sup> However, a CT scan may be indicated to evaluate for pulmonary embolism, if indicated by clinical presentation, because symptoms can mimic COVID-19—related respiratory symptoms and severe illness can increase the risk for venous thromboembolism (VTE).

### Medical management

Pregnant women admitted to the hospital with known or suspected COVID-19 should be monitored for signs of worsening respiratory distress or complications of the disease.

**TABLE 2**

#### Admission criteria for COVID-19 pregnant women and PUIs

##### Clinical

- ☐ Severe shortness of breath
- ☐ Tachypnea (>20 breaths per minute)
- ☐ Hypoxia ( $O_2$  of saturation <95% on room air with ambulation)
- ☐ Pneumonia on imaging
- ☐ Severe asthma
- ☐ Serious comorbidities (eg, cancer, HIV infection, type I diabetes mellitus)

##### Laboratory

- ☐ Elevated C-reactive protein
- ☐ Elevated procalcitonin
- ☐ Platelet count <100,000/ $\mu$ L
- ☐ Elevated prothrombin time
- ☐ D-dimer >3  $\mu$ g/mL
- ☐ Elevated liver function tests

This is suggested admission criteria for pregnant women. If the patient meets any of the following criteria, admission should be considered on a case-by-case basis, taking into account the full clinical picture.

COVID-19, coronavirus disease 2019; PUIs, patients under investigation.

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**TABLE 3**

#### Checklist for the initial management and evaluation of PUIs for COVID-19

1. Nurse dons appropriate PPE (mask, isolation gown, face shield or goggles, and gloves).
2. Nurse places a mask on the patient and visitor.
3. Nurse escorts the patient to the private room (does not need to be negative pressure), and the door is kept closed at all times.
4. Place droplet and contact isolation notifications on the door.
5. Place isolation cart with PPE outside the door.
6. Minimize number of staff who enter the room—only 1 doctor and 1 nurse should evaluate and provide care for the patient.
7. Order the following laboratory tests:
  - CBC, with differential
  - Basic metabolic panel
  - Liver function tests
  - Magnesium
  - Phosphorous
  - PT, PTT, fibrinogen, and D-dimer
  - CRP
  - Respiratory pathogen test—send 1 or multiple of the following per your hospital's guidelines:
    - SARS-CoV-2 test
    - Influenza
    - Respiratory pathogen panel
8. Order chest x-ray (CDC recommends portable device to reduce exposure risk)

Initial management and suggested admission order set, including laboratory and imaging, for newly admitted patients.

CBC, complete blood cell count; CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; PPE, personal protective equipment; PT, prothrombin time; PTT, partial thromboplastin time; PUIs, patients under investigation; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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**TABLE 4**

## COVID-19 in pregnancy management after admission checklist

### Orders

- ☐ Contact and droplet isolation (airborne isolation if patient requires high-flow NC or nebulizers)
- ☐ Vital signs: if stable, obtain every 4 hours at minimum; if unstable, consider continuous monitoring
- ☐ Fetal monitoring: at least once daily for NST as appropriate
- ☐ Admission laboratory tests: CBC, BMP, LFTs, magnesium, phosphorous, PT, PTT, fibrinogen, D-dimer, and CRP
- ☐ Daily laboratory tests: CBC, BMP, LFTs, magnesium, and phosphorus
- ☐ Every other day laboratory tests: CRP, LDH, and D-dimer
- ☐ Anticoagulation and sequential compression devices

### Supportive care

- ☐ Supplemental oxygen to maintain a saturation of  $\geq 95\%$
- ☐ Antipyretics
- ☐ Avoid fluid overload
  - If the patient requires continuous infusion, try to keep it  $< 75$  cc/h.
  - If septic or hemodynamically unstable, give fluids per protocol.

### Medical management

Consider initiating if the patient has 1 of the following:

- ☐ Requires supplemental oxygen
- ☐ Has significant labored breathing
- ☐ Has severe comorbidities

Given rapidly changing guidelines, consideration should be based on institutional guidelines and consultation with infectious disease specialists.

Order set and supportive care medical checklist.

BMP, basic metabolic panel; CBC, complete blood cell count; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; LDH, lactate dehydrogenase; LFT, liver function test; NC, nasal cannula; NST, nonstress test; PT, prothrombin time; PTT, partial thromboplastin time.

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**TABLE 5**

## Tip sheet: hypoxia in pregnant patients with COVID-19

Supplemental oxygen (amount of oxygen delivered by each modality is modifiable and can be adjusted to patient's needs; goal,  $O_2 \geq 95\%$ ):

NC 2–9 L → NRB 10–15 L → move to a negative pressure room

High-flow NC → CPAP → Intubation → ECMO

### Acute decompensation (modify based on severity):

- ☐ Consider repeating baseline admission laboratory tests (CBC, BMP, LFTs, magnesium, phosphate, PT, PTT, fibrinogen, CRP, LDH, and D-dimer).
- ☐ Add procalcitonin.
- ☐ Assess for signs of cardiac injury (troponin and BNP) and consider echo.
- ☐ Assess acid base status.
- ☐ Continuous fetal monitoring as a sixth “vital sign”
- ☐ Monitor hourly intake and output.
- ☐ Assess for bacterial superinfection (repeat CXR, sputum culture, or blood culture).
- ☐ Left lateral vs prone positioning as tolerated

### Antenatal corticosteroids:

- Weigh risk for potential worsening respiratory status vs potential fetal benefit.
- Consider if 24 0/7 to 33 6/7 weeks' gestation and preterm delivery anticipated within 7 days.
- Do not recommend if  $> 34$  weeks' gestation.

### Delivery:

- Multidisciplinary and individualized decision
- $< 34$  weeks' gestation
  - ☐ Maternal risk for decompensation needs to be weighed against fetal benefit of prolonging pregnancy
- $> 34$  weeks' gestation
  - ☐ Consider delivery if acute respiratory distress despite supportive care or presence of significant comorbidities increasing risk for decompensation.

Checklist for pregnant women with hypoxia and acute decompensation (defined as rapidly increasing supplemental oxygen need to maintain  $O_2 \geq 95\%$ ).

BMP, basic metabolic panel; BNP, B-type natriuretic peptide; CBC, complete blood cell count; COVID-19, coronavirus disease 2019; CPAP, continuous positive airway pressure; CRP, C-reactive protein; CXR, chest x-ray; ECMO, extracorporeal membrane oxygenation; LDH, lactate dehydrogenase; LFT, liver function test; NC, nasal cannula; NRB, nonrebreather mask; PT, prothrombin time; PTT, partial thromboplastin time.

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**TABLE 6****Antepartum service management tips**

Antepartum service management tips:

- Create a contact list of key consultants and administration liaisons (nursing administration, neonatology, infectious disease, critical care, and pulmonology).
- Round efficiently:
  - ☐ Avoid preroaming by house staff to decrease healthcare worker exposure.
  - ☐ See patients in the following order:
    1. SARS-CoV-2—negative patients and COVID-19—negative patients
    2. Patients under investigation for COVID-19
    3. Confirmed patients with COVID-19
 This is to decrease chance of transmission and help conserve PPE as needed.
  - ☐ Use in-room media to aid rounding, for example:
    - One person outside of the patient room is stationed at a computer to check laboratory test results, write notes, and enter orders while on speaker phone with the team in the room.
    - The provider stationed at a computer keeps the team in the room informed of pertinent details because handoff sheets and other reference materials cannot be easily or safely accessed while donning full PPE in the patient's room.
- Obtain ambulatory pulse oximetry measurements (walk test) for stable patients as part of the physical examination—patients may seem deceptively well without exertion.
- Pocket ultrasounds for biophysical profiles may be useful for patients with COVID-19 as an alternative to nonstress tests to limit the number of providers entering the room.

Tips for improving efficiency and decreasing staff exposure during COVID-19 pandemic.

COVID-19, coronavirus disease 2019; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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These include pneumonia, hypoxemic respiratory failure or acute respiratory distress syndrome (ARDS), sepsis and septic shock, cardiomyopathy and arrhythmia, acute kidney injury, and complications from prolonged hospitalization, such as bacterial superinfections and VTEs. It is worth noting that worsening of symptoms may occur 6 to 10 days after the onset of symptoms.<sup>1</sup>

Medical care is largely focused on infection prevention and control measures and supportive care. Several medical therapies have been proposed to aid in the treatment for COVID-19 including hydroxychloroquine, remdesivir, interleukin-6 (IL-6) inhibitors, and convalescent plasma. Although multiple clinical trials are investigating the safety and efficacy of these treatments, currently none have been approved by the US Food and Drug Administration (FDA). Continuous review of the literature is needed given the rapidly changing guidelines, and consultation with infectious disease specialists may be warranted before initiation of medical management.

Based on promising data from in vitro studies and 1 small nonrandomized clinical study, chloroquine or hydroxychloroquine<sup>13–15</sup> quickly became the first-line therapy for many hospitalized patients with COVID-19, despite the lack of high-quality data proving its efficacy in humans. Its use can be considered based on institutional guidelines and consultation with infectious disease specialists. Hydroxychloroquine is most commonly used in pregnancy for the treatment for maternal lupus and is used outside of pregnancy to primarily treat rheumatoid arthritis, systemic lupus erythematosus, and malaria. Although it can be detected in the cord blood and breast milk,<sup>16</sup> no human studies have reported adverse fetal effects.<sup>17</sup> Hydroxychloroquine is generally considered safe in pregnancy and during breastfeeding.

Prolonged QT interval may be a side effect of hydroxychloroquine. It should be used with caution in patients with hepatic or renal dysfunction or when used in combination with other drugs that may prolong QT intervals owing to increased risk for arrhythmia. Before treatment with hydroxychloroquine, a baseline electrocardiogram should be obtained to assess the QT interval and treatment should not be initiated if the corrected QT interval is greater than 500 ms. The package insert for hydroxychloroquine suggests an increased risk for hemolytic anemia in patients with a glucose-6-phosphate dehydrogenase (G6PD) deficiency.<sup>18</sup> Consideration should be given to G6PD testing, but testing should not delay initiation of treatment. Optimal dosing and duration of hydroxychloroquine for treatment for COVID-19 are unknown. Anecdotal dosing options are 400 to 600 mg orally every 12 hours for 24 hours, followed by 400 mg orally every 24 hours for 4 to 5 days.<sup>1</sup>

Other treatments under investigation include remdesivir, IL-6 inhibitors, and convalescent plasma. Recently, the FDA issued an emergency use authorization for remdesivir, which is an investigational antiviral medication, for inpatient treatment of patients with severe COVID-19.<sup>19</sup> Per the CDC, to date there are insufficient data to recommend the use of convalescent plasma or IL-6 inhibitors, although clinical trials are ongoing.<sup>1</sup>

#### Corticosteroid use

Corticosteroid use in the setting of COVID-19 should be approached cautiously. The CDC currently states that steroid use should be avoided unless indicated for other reasons, such as asthma or reactive airway disease, chronic obstructive pulmonary disease, fetal lung maturity promotion, or refractory septic shock. This recommendation is due to the potential of

TABLE 7

## Reference ranges for common COVID-19 laboratory tests

Laboratory test	Nonpregnant	First trimester	Second trimester	Third trimester
WBC ( $\times 10^3/\text{mm}^3$ )	3.50–9.10	5.70–13.60	5.60–14.80	5.90–16.90
Platelet ( $\times 10^9/\text{L}$ )	165.00–415.00	174.00–391.00	155.00–409.00	146.00–429.00
D-dimer ( $\mu\text{g/mL}$ )	0.22–0.74	0.05–0.95	0.32–1.29	0.13–1.70
Ferritin (ng/mL)	10.00–150.00	6.00–130.00	2.00–230.00	0.00–116.00
CRP (mg/L)	0.20–3.00	Not reported	0.40–20.30	0.40–8.10
Procalcitonin ( $\mu\text{g/mL}$ )	0.01–0.15	0.018–0.051	0.018–0.051	0.02–0.15
Fibrinogen (mg/dL)	233.00–496.00	244.00–510.00	291.00–538.00	373.00–619.00
PT (s)	12.70–15.4	9.70–13.50	9.50–13.40	9.60–12.90
PTT (s)	26.30–39.40	24.30–38.90	24.20–38.10	24.70–35.00
INR	0.90–1.040	0.89–1.05	0.85–0.97	0.08–0.94
AST (U/L)	12.00–38.00	3.00–23.00	3.00–33.00	4.00–32.00
ALT (U/L)	7.00–41.00	3.00–30.00	2.00–33.00	2.00–25.00
LDH (U/L)	115.00–221.00	78.00–433.00	80.00–447.00	82.00–524.00
Magnesium (mg/dL)	1.50–2.30	1.60–2.20	1.50–2.20	1.10–2.20
Phosphate (mg/dL)	2.50–4.30	3.10–4.60	2.50–4.60	2.80–4.60
Troponin I (ng/mL)	0.08	Not reported	Not reported	0–0.064
Creatine kinase (U/L)	39.00–238.00	27.00–83.00	25.00–75.00	13.00–101.00
BNP (pg/mL)	<167	Not reported	13.50–29.50	Not reported
pH (venous)	7.31–7.41	7.36–7.52	7.40–7.52	7.41–7.53
pO <sub>2</sub> (mm Hg)	90.00–100.00	93.00–100.00	90.00–98.00	92.00–107.00
pCO <sub>2</sub> (mm Hg)	38.00–42.00	Not reported	Not reported	25.00–33.00
HCO <sub>3</sub> <sup>-</sup> (mEq/L)	22.00–26.00	Not reported	Not reported	16.00–22.00

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, B-type natriuretic peptide; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; INR, international normalized ratio; LDH, lactate dehydrogenase; PT, prothrombin time; PTT, partial thromboplastin time; WBC, white blood cell count.

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corticosteroids to prolong viral replication, which has been observed with MERS, coronavirus, and influenza infections.<sup>1</sup> The Infectious Diseases Society of America also suggests against the use of steroids for patients admitted to the hospital with COVID-19 pneumonia. However, they recognize a potential benefit for patients who progress to ARDS because of COVID-19, in the context of a clinical trial.<sup>20</sup>

In pregnant women with a history of asthma, inhaled corticosteroids are preferred for mild to moderate symptoms, along with an inhaled beta agonist when indicated. Metered-dose inhalers are preferred over nebulized treatments, which can aerosolize viral particles and increase viral spread. Institutions may want to prioritize nebulized treatments for patients without COVID-19 with asthma to ensure availability of inhalers for patients with COVID-19. If a patient requires a treatment with nebulizer, then airborne precautions must be taken. Should inhaled steroids fail to resolve the symptoms, systemic corticosteroids may be administered to pregnant women with asthma with a positive result for SARS-CoV-2 if necessary.

Antenatal corticosteroids for fetal lung maturity may be considered for pregnant women with suspected or confirmed COVID-19 who are between 24 0/7 and 33 6/7 weeks' gestation and at risk for preterm birth within 7 days. The theoretical risk for prolonged maternal infection and potential decompensation after systemic steroids needs to be weighed against the potential fetal benefit. ACOG does not recommend offering antenatal corticosteroids to pregnant patients with suspected or confirmed COVID-19 who are beyond 34 0/7 weeks' gestation.<sup>21</sup>

#### Antibiotic therapy for bacterial pneumonia

Antibiotic therapy for bacterial pneumonia is generally not indicated when the clinical findings are consistent with viral pneumonia. However, antibiotic therapy may be warranted in the setting of atypical chest x-ray findings (eg, a single area of consolidation), risk factors for aspiration, or risk factors for superimposed bacterial pneumonia. Sputum cultures, blood cultures, and elevated procalcitonin may be helpful in the diagnosis of superimposed bacterial pneumonia. In addition,

initiation of antibiotic treatment may have a role when clinical suspicion or disease severity is high (eg, prolonged intubation). Clinical judgment based on patient presentation along with consideration for the safety profile in pregnancy should be used in the selection of the type of antibiotic medication.

#### Anticoagulation

Coagulopathy and disseminated DIC resulting in microvascular thrombosis and coagulation factor consumption have been seen in nonpregnant patients with COVID-19. Laboratory values may indicate low platelet counts, prolonged prothrombin time (PT), elevated D-dimer, and low fibrinogen levels, which may mimic HELLP syndrome and preeclampsia with severe features. More than 70% of nonpregnant patients with fatal COVID-19 met the criteria for DIC compared with less than 1% in patients with nonfatal disease.<sup>22</sup> The International Society on Thrombosis and Haemostasis recommends measuring D-dimer levels, PT, and platelet count in all patients with confirmed or suspected COVID-19.<sup>23</sup> Although abnormal coagulation profiles are common in patients with COVID-19, bleeding has not been a major finding. Therefore, some have recommended using D-dimer, whereas others use the overall clinical picture to determine an anticoagulation approach.

If using D-dimer approach, prophylactic anticoagulation has been recommended for those with D-dimer level of  $<3.0 \mu\text{g/mL}$  and therapeutic anticoagulation for those with D-dimer level of  $>3.0 \mu\text{g/mL}$ <sup>9</sup> in nonpregnant patients. D-dimer levels increase in pregnancy, particularly in the third trimester (Table 7). In nonpregnant women, D-dimer level ranges from 0.22 to  $0.74 \mu\text{g/mL}$  whereas in the third trimester, levels range from 0.13 to  $1.7 \mu\text{g/mL}$ .<sup>24</sup> The threshold for the level of D-dimer that should raise concern in pregnancy is not known, but consideration of prophylactic or therapeutic anticoagulation based on the given clinical circumstances is critical, if no contraindication exists (eg, active bleeding or severe thrombocytopenia). This may be most relevant for symptomatic patients, particularly those with thrombocytopenia or an abnormal coagulation profile. It should be noted that abnormal PT or partial thromboplastin time is not a contraindication to anticoagulation, and the full clinical picture should be taken into account.

While admitted to the hospital, VTE prophylaxis for pregnant women with COVID-19 should be universally employed when delivery is not imminent. The decision for therapeutic anticoagulation is considered on a case-by-case basis based on disease severity and clinical parameters. In pregnancy, the timing of delivery and the risk for intrapartum hemorrhage must be considered.

Finally, the duration for anticoagulation owing to COVID-19 in pregnancy and the postpartum period is not known. Given the well-known procoagulant state in the postpartum period, some institutions have initiated anticoagulation up to 4 to 6 weeks in the postpartum period for some high-risk women. Clinical judgment is necessary given the lack of data-driven protocols.

#### Delivery

##### Timing of delivery

A diagnosis of COVID-19 alone is not an indication for delivery.<sup>21,25</sup> In cases wherein women recover from COVID-19 and have no other medical indications for delivery, it is reasonable to postpone delivery until the quarantine status is lifted, to avoid transmission to the neonate.<sup>21</sup> Delivery after this period should be for usual obstetrical indications.

Delivery timing in the preterm patient with acute respiratory distress poses unique challenges, and care should be individualized. Given that the risks for prematurity after 34 weeks' gestation are typically minimal, the threshold for delivery may be lower than that before 34 weeks' gestation, particularly in the setting of acute respiratory distress or significant comorbidities that may increase the risk for maternal decompensation. In patients at 24 0/7 to 33 6/7 weeks' gestation, prolonging pregnancy for fetal benefit needs to be weighed against the maternal risk for decompensation. The lack of clear evidence that evacuation of the uterus will improve maternal respiratory function in women with acute respiratory failure from COVID-19 pneumonia complicates decision making. In the setting of worsening maternal respiratory status and potential for deterioration, an interdisciplinary discussion should be held between obstetrics, anesthesiology, pulmonary and critical care, pediatrics, and nursing, together with the patient and her family.<sup>25</sup>

##### Mode of delivery

The diagnosis of COVID-19 alone is not an indication for cesarean delivery.<sup>21</sup> In cases wherein the risk for respiratory decompensation seems low, it is reasonable to allow spontaneous labor or attempt induction of labor to achieve a vaginal delivery if no other contraindications exist. An assisted second stage may be necessary if the patient has severe dyspnea or hypoxia after a Valsalva maneuver. A simple walk test can provide helpful information on the patient's exercise tolerance before the induction of labor. For moderate to severe cases of respiratory distress, the risks associated with surgery need to be balanced against the risk for respiratory decompensation in labor.

It is prudent to avoid intubation if clinically possible, owing to both the risk for aerosolization and the inherent increased risks for intubation in the pregnant state. Pregnancy is associated with increased upper airway edema and rapid oxygen desaturation that are worsened with respiratory distress in COVID-19. Thus, we recommend early epidural anesthesia when appropriate to minimize the need for general anesthesia in the event of an emergent cesarean delivery.<sup>26</sup>

##### Vertical transmission and fetal effects

Currently, case reports suggest that vertical transmission may occur; however, the rate of vertical infection and the clinical effect on the fetus or newborn are not clear.<sup>27</sup> It is not clear whether the transmission to the newborns occurred antenatally, during the delivery, or as a result of neonatal exposure. Vertical transmission has not been reported for MERS and



SARS.<sup>1</sup> Consideration should be taken to send all placentas from mothers with positive results for COVID-19 to pathology for evaluation. This will add an additional source of information regarding vertical transmission and how the virus may affect pregnancy.

To date, no evidence of teratogenic effects of COVID-19 has been reported. However, there currently are no data to inform possible long-term teratogenic effects because SARS-CoV-2 has only been present since December 2019. Of note, 1 case report described a fetal demise in the setting of a critically ill mother with COVID-19.<sup>28</sup>

### Acute decompensation

#### Oxygenation goals

The fetus requires a maternal PaO<sub>2</sub> of >70 mm Hg for sufficient oxygenation. Maternal hypoxia and hypocapnia result in fetoplacental vasoconstriction, which is poorly tolerated by the fetus. Thus, maternal oxygenation goals include SpO<sub>2</sub> of ≥95% or PaO<sub>2</sub> of ≥70 mm Hg.<sup>3</sup> Electronic fetal monitoring may be useful as a maternal vital sign and a continuous indication of maternal oxygenation status. Fetal monitoring should also be used when fetal intervention, including delivery, would be considered.<sup>8</sup>

#### Intubation and mechanical ventilation

Intubation should be a multidisciplinary and individualized decision. Indications for intubation include apnea, inability of the patient to protect her airway, PaO<sub>2</sub> of <70 mm Hg on supplemental oxygen of higher than 50%, elevated and rising PaCO<sub>2</sub> (reference values are provided in Table 7), increased work of breathing, mental status deterioration, and hemodynamic instability.<sup>29</sup>

Intubation carries a significant risk owing to the physiological changes of pregnancy. Endotracheal intubation when necessary should be performed in as controlled an environment as possible. Increased rates of intubation failure in pregnancy are caused by upper airway edema and hyperemia and rapid oxygen desaturation after apnea.<sup>30</sup> There is also an increased risk for aspiration owing to reduced tone of the lower esophageal sphincter, increased abdominal pressure, and delayed gastric emptying.<sup>3</sup>

Because of the decreased oxygen reserve in pregnancy, secondary to decreased functional residual capacity and increased oxygen consumption, intubation should be performed with 100% O<sub>2</sub> preoxygenation, with rapid sequence induction (without ventilation via a face mask), and with cricoid pressure.<sup>3</sup> Given the risk for aerosolization of the virus, intubation should ideally be performed in a negative pressure room, and all providers should don appropriate personal protective equipment including an N95 mask.

Mechanical ventilation settings in pregnancy should include higher peak inspiratory pressure and positive end-expiratory pressure. Hyperventilation should be avoided to prevent subsequent respiratory alkalosis that can induce decreased uterine blood flow.<sup>3,29</sup> PaCO<sub>2</sub> should not be lower than 30 mm Hg (normal physiological range of pregnancy: 30–32 mm Hg).

Tidal volumes should be initiated at 4 to 6 mL/kg of lean body weight.<sup>3</sup> Treatment for ARDS in pregnancy follows the same guidelines as in nonpregnant patients: lung-protective ventilation, anti-infectious medications, and supportive therapy.<sup>3,31</sup>

#### Cardiopulmonary failure

Several physiological and anatomic changes in pregnancy make the pregnant patient susceptible to cardiopulmonary failure.<sup>3</sup> These include increased cardiac demands owing to increased cardiac output, the mechanical effects of the gravid uterus, and the increased metabolic demands of pregnancy.

Patients with COVID-19 should be monitored for signs of cardiac dysfunction and pulmonary edema. If there is a concern, an echocardiogram should be performed to assess left ventricular function. The treatment for pulmonary edema includes supplementation with oxygen and diuretics, along with inotropic agents and pressure support to maintain mean arterial pressure of >65 mm Hg in the setting of cardiac failure.

#### Postpartum management

Delivery does not always improve the respiratory status of a pregnant patient with COVID-19, and acute respiratory decompensation remains a risk in the postpartum period. Supportive care remains the mainstay of management with continuation of any medical management initiated antenatally or intrapartum. In addition, consideration of anticoagulation in severely ill patients is warranted.<sup>8</sup> A duration of 4 to 6 weeks could be considered given the known heightened thrombotic risk.

#### Nonsteroidal anti-inflammatory drugs

It has been hypothesized that nonsteroidal anti-inflammatory drugs (NSAIDs) may worsen COVID-19 because they cause increased angiotensin-converting enzyme 2 (ACE2) expression and the coronavirus binds cells through the ACE2 receptor.<sup>32</sup> However, clinical data thus far have not validated this theory. SMFM, ACOG, and the FDA have not restricted NSAID use in patients with COVID-19.<sup>21,33,34</sup> We recommend that women who are asymptomatic or mildly symptomatic can continue to use NSAIDs as needed. However, it is reasonable to avoid NSAIDs in severely symptomatic patients given the theoretical risk.<sup>33</sup>

#### Breastfeeding

COVID-19 infection is not a contraindication to breastfeeding.<sup>25,35</sup> Studies to date have not detected coronavirus in breast milk. Breastfeeding should be encouraged because it likely provides antibodies against the coronavirus for the infant. Mothers who wish to directly breastfeed should wear a mask, perform strict hand hygiene, and wash their breasts with soap and water before feeding<sup>1</sup> to avoid neonatal acquisition via respiratory droplets. Alternatively, mothers may use a breast pump and a healthy caregiver can bottle-feed the infant until the mother is no longer quarantined. All components of the breast pump must be cleaned thoroughly between pumping sessions.

## Discharge and follow-up

Clinical recovery has been correlated with the detection of immunoglobulin (Ig) M and IgG antibodies suggesting immunity; however, there are limited data on the possibility of reinfection.<sup>1</sup>

Ongoing transmission seems to occur up to approximately 7 days after the initial presentation of symptoms. Thus, appropriate counseling about quarantining the patient and her contacts should be provided based on CDC recommendations. Briefly, after 72 hours of being afebrile without the use of fever-reducing medication and improvement in symptoms and at least 7 days have passed since symptoms first appeared, isolation can be discontinued.<sup>1</sup> After the isolation period, patients should continue to practice proper hygiene protocols and avoid contact with vulnerable persons.

Similar to pregnant patients with COVID-19, postpartum patients with COVID-19 may also initially be stable or improve and later develop worsening symptoms. Therefore, consideration should be given to discharging the postpartum patient with a pulse oximeter and clear parameters to trigger either a call to a provider or a return to the hospital. A list of postpartum patients with COVID-19 should also be maintained. The patients should be contacted regularly via telephone call, text, or video call to provide patient education and identify patients needing physician evaluation or hospital admission. This should be continued until complete resolution of the patient's signs and symptoms of infection.

## Conclusion

The speed of the emergence and spread of COVID-19 around the world has placed an incredible strain on healthcare staff and resources, particularly in the field of obstetrics. The key to responding to this crisis is thoughtful, standardized, and evidence-based care whenever possible. This article contained suggestions for management. However, as more evidence accumulates, guidance will inevitably change. ■

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